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(54) Title: ION VAPOR SOURCE FOR MASS SPECTROMETRY OF LIQUIDS

(57) Abstract

A process for generating an ion vapor from a liquid sample can be used in interfacing a liquid chromatograph (9) to a mass spectrometer (4). The process includes generating an aerosol from the liquid. Preferably at least a fraction of the particles in the aerosol are charged. The process includes impacting the particles against a surface (46) which is maintained at a temperature above an impact-vaporization temperature. Upon colliding with the surface the particles are vaporized and an ion vapor formed.

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Description

Ion Vapor Source for
Mass Spectrometry of Liquids

5

Government Support

Technical Field

The present invention relates to the field of
15   mass spectrometry. More particularly, the invention
relates to a method and apparatus for generating an ion
vapor from a liquid sample for analysis by a mass analyzer
such as a quadrupole mass spectrometer. The invention is
especially suited to interface a liquid chromatograph to a
20   mass spectrometer.

Background Art

The information in the mass spectrum of a chemical
25   compound is of great value to chemists in identifying the
compound and in characterizing its molecular structure.
For those compounds for which mass spectra can be obtained,
the mass spectrum typically reveals the molecular weight
of the compound and the masses of a characteristic assortment
30   of ionic fragments derived from the compound. To generate
mass spectra, conventional mass spectrometers operate on
a beam of ions derived from the material to be analyzed,
either by deflecting the beam electromagnetically in a way
which depends upon the ratio of the mass to the charge of

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the ions in the beam, or by measuring transit times of
ions in a pulsed ion beam. Compounds which are to be mass
analyzed generally must be converted into an ion vapor

5   before introduction into the section of a conventional
mass spectrometer which forms the ion beam.

The need to convert materials to be mass analyzed
into an ion vapor has been a source of problems in the

10   field of mass spectrometry for which no completely
satisfactory solution has heretofore existed. Gaseous
compounds or compounds which can be thermally vaporized
without decomposition can usually be converted to an ion
vapor relatively easily by heating the compound to

15   vaporize it if it is not a gas, and either bombarding the
compound in the gaseous state with a beam of electrons
(electron impact ionization) or by introducing chemically-
reactive ions into the gas (chemical ionization). However,
many compounds are not sufficiently volatile at ambient

20   temperatures to form a gas suitable for either electron-
impact ionization or chemical ionization, and, moreover,
decompose when heated so that they cannot be vaporized
thermally. Among the compounds which cannot be converted
into an ion vapor by these conventional techniques are

25   many which are of biological, medical and pharmaceutical
interest.

A number of special techniques have been
developed to generate an ion vapor from compounds of low

30   volatility. These techniques include field desorption,
laser-assisted field desorption, plasma desorption, rapid
evaporation from inert surfaces, and secondary ionization
mass spectrometry. Literature citations to these and other
techniques may be found in Analytical Chemistry, vol 51,

35   pp. 682A-701A (June 1979). None of these techniques is
without its limitations, however, and a need still exists

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for improved methods for obtaining mass spectra of
involatile, heat-sensitive materials.

The problems of forming an ion vapor of involatile
5   and heat-sensitive compounds become particularly acute
when it is attempted to use a mass spectrometer to analyze
the effluent of a liquid chromatograph. Liquid chromato-
graphs are widely used to separate mixtures into their
component compounds, and find particular application when
10   one or more of the component compounds is too involatile
to permit the mixture to be separated with a conventional
gas chromatograph. Although mass spectrometers have been
widely and successfully interfaced to gas chromatographs to
permit mass spectra to be taken of compounds in the gaseous
15   effluent from the chromatograph, efforts to interface
liquid chromatographs to mass spectrometers have been
less successful, in part because compounds eluted from the
liquid chromatograph are frequently involatile and heat
sensitive and thus not amenable to conversion into an ion
20   vapor by conventional techniques. Moreover, the compounds
to be analyzed from the liquid chromatograph are dissolved
in a volatile solvent, which tends to reduce the ionization
efficiency of the mass spectrometer even further with
respect to the solute compounds of interest since solvent
25   vapor is generally ionized along with the solute compounds
and the solvent is typically in a much greater concentration
than the solute compounds.

One attempt to interface a mass spectrometer to a
30   liquid chromatograph is described in United States Patent
No. 4,160,161 to Horton. Effluent from a liquid chromato-
graph is injected into an ion chamber maintained at a low
pressure by means of a needle which projects into the
chamber. The low pressure in the chamber, approximately
35   10^{-3} atmospheres, pulls the solvent and solute through

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the needle and sprays it into the chamber. A laser or
other heat source may be utilized to prevent the effluent
from freezing as it flows through the needle and to pro-
vide heat to the effluent in the ion chamber. The needle
5   is maintained at a high voltage by a high voltage power
supply so that droplets of spray carry a charge. The
solvent evaporates in the low pressure environment,
reducing the size of the charged droplets until ideally
only the ions remain. In devices illustrated in Figures 1
10 and 3 of the '161 patent, the ions travel in an unob-
structed straight-line path through differentially pumped
chambers and finally into an ion mass selector of the mass
spectrometer system. In an apparatus illustrated in
Figure 2, ions must be deflected electrostatically to pass
15 through the differentially pumped chambers and into the
ion mass selector.

The apparatus of the '161 patent has a serious
drawback associated with the application of a high voltage
20 to the needle projecting into the ion chamber. At the
reduced pressure employed in the ion chamber approximate-
ly 10^{-3} atmospheres, gases and vapors in the presence of
high voltages tend to break down readily and become elec-
trically conductive. As a result, uncontrolled electrical
25 discharges are likely to occur in the ion chamber, lead-
ing to unstable and erratic behavior. A further problem
would arise if the effluent solution from the liquid
chromatograph were electrically conductive, as would be
the case in reversed-phase liquid chromatography when
30 aqueous buffers are used. If such conductive solutions
were introduced into the needle maintained at a high
voltage, substantial electrical current would flow through
the solution between the needle and the liquid chromato-
graph, even if the conduit connecting them were made of
35 an insulating material. Such a current flow could cause

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electrolysis of the solution and other uncontrolled
effects.

Disclosure of Invention

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    We have invented an improved ion vapor source and
process which permits an ion vapor to be generated effi-
ciently from a large class of liquid samples, including in
many instances solutions of involatile and heat-sensitive
10 compounds such as might be eluted from a liquid chromatograph,
and which avoids the problems in the prior art noted
above.

    Broadly, the process of the invention concerns
15 generating an aerosol from a liquid sample in which
a fraction of the particles in the aerosol may be elec-
trically charged. As used herein, the term "particle"
encompasses liquid droplets and solid particles, but,
consistent with conventional usage, does not encompass
ions or molecules in a gaseous phase. The aerosol can be
20 generated by metering the liquid into a capillary passage-
way and heating the walls of a length of the passageway
sufficiently strongly to atomize the liquid to a mixture
including vapor and particles. The process of the inven-
tion further includes the step of maintaining a vapori-
25 zation surface, preferably located in a region maintained
at a subatmospheric pressure, at a temperature above an
impact-vaporization temperature of the particles. The
process further includes the step of directing at least a
fraction of the particles to impinge upon the vaporization
30 surface. Upon colliding with the surface the particles
are vaporized and an ion vapor formed. Electric charge to
form the ions is preferably carried by the particles
striking the vaporization surface. Alternatively, charge
may be generated at the surface in the impact vaporization
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process in certain cases. If desired, vapor from the
vaporization surface can be ionized using conventional
chemical or electron impact ionization.

5   Surprisingly, many involatile chemical compounds
which decompose rather than vaporize when heated can be
converted by preferred embodiments of the present
nvention into an ion vapor suitable for analysis by a
mass spectrometer. The mass spectrum of an ion vapor so
10   produced generally exhibits little evidence of pyrolytic
decomposition and, moreover, generally exhibits relatively
little of the ion fragmentation characteristic of mass
spectra obtained using the conventional electron impact
ionization technique. The process of the invention can
15   therefore be termed a "soft" ionization technique.

When a mixture of aerosol and vapor is generated
from a solution by strongly heating the walls of a length
of a capillary passageway and metering the solution into
20   the passageway, it is generally found that solutes which
are less volatile than the solvent are preferentially
contained in the particles of the aerosol. Furthermore,
particularly when using polar solvents, it is found that
particles of the aerosol are electricaly charged, even
25   when no electrical voltages are applied. If the capillary
passageway is linear, the particles of the aerosol ejected
from the passageway tend to form a beam with a relatively
large component of the momentum of the particles directed
along an axis of the passageway, as compared to components
30   of momentum transverse to the axis. As a result, the beam
of particles tends to be contained in a narrow cone about
the axis of the passageway, which facilitates directing a
substantial fraction of the particles ejected from the
passageway against the vaporizer surface.
35

A preferred ion vapor source capable of carrying
out the process of the invention on liquid samples for a
mass spectrometer includes a housing attached to the mass
spectrometer. The housing is generally vacuum tight with
5 the interior of the housing defining a vacuum chamber. An
evacuation port opens into the vacuum chamber and is
connectable to a vacuum pump for maintaining the vacuum
chamber at a subatmospheric pressure. It is preferred to
maintain the pressure in the vacuum chamber in a range of
10 from about 0.1 torr to about 10 torr. In addition, the
housing has an inlet port and an ion-vapor discharge
orifice which communicates between the vacuum chamber and
an ion vapor inlet of the mass spectrometer.

15   The ion vapor source also includes an atomizing
nozzle assembly which is secured to the inlet port of the
housing to form a vacuum-tight seal. A passageway extends
through the atomizing nozzle assembly for introducing a
liquid sample into the vacuum chamber. A first end of the
20 passageway defines a liquid sample inlet for receiving the
liquid sample. For example, the nozzle assembly could be
connected to a liquid chromatograph to permit liquid
samples eluted from the chromatograph to flow into the
liquid sample inlet of the nozzle assembly. A second end
25 of the passageway which opens into the vacuum chamber
defines a spray outlet for discharging an atomized
spray of vapor and particles of the sample into the
chamber. A nozzle heater is provided for heating at least
a portion of the nozzle assembly sufficiently strongly to
30 heat the liquid sample flowing in the passageway to
atomize the sample. An electrical resistance heater or
oxy-hydrogen torches capable of heating the atomizing
nozzle assembly to incandescence are preferred nozzle
heaters.

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The ion vapor source also includes a surface
vaporizer for intercepting particles of sample for vapori-
zation. The surface vaporizer includes a vaporizer
surface located within the vacuum chamber in the vicinity
5 of the ion-vapor discharge orifice. The vaporizer surface
is positioned and oriented so that at least a fraction of
the particles discharged from the spray outlet of the
nozzle assembly are intercepted by the vaporizer surface.
The vaporizer surface can be heated to an impact-vaporiza-
10 tion temperature by a surface vaporizer heater such as an
electrical-resistance heating element in thermal contact
with the vaporizer surface. Particles of sample impinging
upon the surface can be vaporized to form an ion vapor for
introduction into the ion-vapor inlet of the mass spectrometer.

15

The ion vapor source of the present invention is
particularly suited to interface a liquid chromatograph to
a mass spectrometer. The effluent from a liquid chromato-
graph is typically a solution of a solute compound at a
20 low concentration in a relatively volatile solvent.
When such a solution is introduced into a mass spectrometer
equipped with a preferred ion vapor source of the present
invention, the mass spectrum obtained generally shows
the solvent peaks to be orders of magnitude lower in
25 intensity relative to the intensity of the solute peaks
than would be expected on the basis of their relative mole
fractions in the solution. The reduced solvent peak
intensity arises in part because under preferred operating
conditions roughly 95 percent of the solvent in the
30 solution is vaporized before the particles of sample
impinge upon the vaporizer surface, thereby concentrating
the solution. Moreover, it appears in many cases that the
electric charges on the particles and whatever additional
charges are picked up at the vaporizer surface are prefer-
35 entially carried by the solute molecules after vaporization
on the vaporization surface.

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Certain solutions of compounds can be ionized
both by embodiments of the present invention which involve
no chemical or electron-impact ionization and by a conven-
tional chemical ionization technique. Mass spectra of
5 such a solution taken using the two ionization techniques
permit the two techniques to be compared. Generally it is
found that the total intensity of the peaks attributed to
the solute is less by one or two orders of magnitude for
spectra taken with the present invention as compared with
10 spectra taken using chemical ionization. However, the
total intensity of the solvent peaks is typically four or
five orders of magnitude lower in intensity for spectra
taken with the present invention as compared to spectra
taken using chemical ionization. Thus in many cases the
15 intensity of the solute ions over the solvent ion back-
ground can be increased with the present invention by two
to four orders of magnitude relative to conventional
chemical ionization.

20   Generally the overall sensitivity of a mass
spectrometer equipped with an ion vapor source of the
present invention depends upon the nature of the liquids
analyzed. In the case of solutions, the nature of the
solvent is a significant factor. Polar solvents such
25 as water and methanol ordinarily provide the best results
for embodiments of the invention which involve no chemical
or electron-impact ionization. Dilute formic acid is
particularly preferred as a polar solvent. Dilute formic
acid is a suitable solvent for many compounds of biological
30 interest and can be used in conventional liquid chroma-
tography. Hexane, a nonpolar solvent, has not given
satisfactory intensities when used with embodiments
of the present invention which involve no electron impact
or chemical ionization. Consequently, when using hexane

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as a solvent, it is preferred to employ a supplemental
ionization technique, such as chemical ionization, subse-
quent to vaporization on the vaporizer surface.

5   Both positive and negative ions can be produced
with embodiments of the present invention which employ a
heated nozzle for atomization and involve no electron-
impact or chemical ionization. Ordinarily, positive
ions are formed more readily in such embodiments, so that
10   positive ion spectra taken using the present invention are
generally more intense than corresponding negative ion
spectra. Charged particles of either polarity can be
generated with the heated atomizing nozzle assembly of the
preferred embodiment of the invention. The polarity
15 depends at least in part on the nature of the liquid
atomized, the temperature to which the nozzle is heated,
and the rate of flow of the liquid through the heated
zone.

20   Preferred ion vapor sources of the present
invention can be inexpensive to manufacture relative to
conventional ion sources used in mass spectrometry. No
high-voltage source or electrostatic deflector is required
to generate an ion vapor in accordance with preferred
25 processes of the invention.

The ion vapor source of the present invention
can operate at pressures as high as about one torr or
even higher. In fact, in certain instances it has been
30 observed that reducing the pressure surrounding the
vaporization surface of an ion vapor source of the present
invention to a high vacuum resulted in a drastically
reduced ionization efficiency. Operation of the ion vapor

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source at pressures as high as one torr or so is a signifi-
cant advantage for liquid samples containing a relatively
volatile solvent, since vacuum pumps with a capacity to
pump away solvent vapor at a rate sufficient to maintain
5   the interior of the source at a preferred pressure of one
torr or so need not have a high-vacuum capability. Vacuum
pumps having both a high-vacuum capability and a high
pumping rate are expensive and bulky.

10 Brief Description of the Drawings

The details of preferred embodiments of the
invention will be described in connection with the accom-
panying drawings.

15
FIG. 1 is a side view in partial section of an
ion vapor source of the present invention connected to a
quadrupole mass spectrometer.

20 FIG. 2 is a side view in partial section of an
atomizing nozzle assembly which employs electrical
resistance heating.

FIG. 3 is a mass spectrum of adenosine 5'-mono-
25 phosphate dissolved in dilute formic acid obtained with
the mass spectrometer system of FIG. 1. The concentra-
tion of the phosphate was about 10 parts per million
relative to the solvent.

30 Best Mode for Carrying Out the Invention

Turning now to FIG. 1, an ion vapor source 2 is
connected to a quadrupole mass spectrometer 4 to supply an
ion vapor to the mass spectrometer for analysis. An
35 atomizing nozzle assembly 5 includes a stainless steel

capillary tube 6 having a capillary passageway 10 extending
through it. The inside diameter of the capillary tube 6
could be about 0.15 mm, for example. The capillary tube 6
is electrically grounded. A liquid chromatograph 9 is

5   connected to the capillary tube 6 for metering liquid
effluent from the chromatograph into the capillary passage-
way 10. Four oxy-hydrogen torches 12 are disposed
symmetrically around the capillary tube 6 at a discharge
end portion 14 of the capillary tube. The discharge end

10   portion of the capillary tube 6 is linear. A particle
beam axis is defined by an axis of the linear discharge
end portion 14. Each of the torches 12 has a burner
tip 13 which is oriented to direct a flame from the torch
against the capillary tube 6. A torch housing 16 surrounds

15   the burner tips 13 of the torches 12. The torch housing
16 is provided with a vent 18 for venting the water vapor
generated by the oxyhydrogen flames of the torches 12.

The passageway 10 of the capillary tube 6
opens into a spray input subchamber 20 which is defined by

20   a generally vacuum-tight spray-input housing 22. The
spray-input housing 22 has a first evacuation port 24
which permits the spray input subchamber 20 to be evacu-
ated. The first evacuation port 24 is connected to a
first vacuum pump (not shown) for maintaining the subcham-

25   ber 20 at a subatmospheric pressure. A frustoconical
skimmer 26 partitions the spray input subchamber 20 from a
surface vaporization subchamber 30. The skimmer 26 has a
pinhole collimator opening 28 passing through it which
permits the spray input subchamber 20 to communicate

30   with the surface vaporization subchamber 30. The collimator
opening 28 is located on the particle beam axis.

The surface vaporization subchamber 30 is defined
by the interior of a tubular surface vaporizer housing 32

35   which has a second evacuation port 34 which is connected
to a second vacuum pump (not shown) for maintaining the

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interior of the surface vaporizer subchamber 30 at a
subatmospheric pressure. An ion-vapor discharge orifice
36 passes through the surface vaporizer housing 32 and
permits communication with the quadrupole mass spec-
5 trometer 4.

A surface vaporization probe 40 includes a support
arm 42 and a surface-vaporizer probe tip 44. The probe
tip 44 is made of nickel-plated copper and has a planar
10 face which defines a vaporizer surface 46. The vaporizer
surface 46 is positioned and oriented to intercept the
the particle beam axis. An electrically-resistive heating
element 48 is located within the interior of the surface-
vaporization probe 40 for heating the vaporizer surface
15 46 to temperatures ranging from ambient temperature up to
about 350°C. If desired, an electron beam generator (not
shown) could be positioned to direct an electron beam to a
region close to the vaporizer surface 46 and the ion vapor
discharge orifice 36 to permit conventional electron
20 impact ionization and chemical ionization to be carried
out in the ion vapor source 2.

The quadrupole mass spectrometer 4 is conven-
tional and will therefore only be described briefly.
25 Accelerating electrodes 50 are positioned close to the
ion vapor discharge orifice 36 of the ion vapor source
to accelerate ions in the ion vapor issuing from the
discharge orifice. A partition 52 having a pinhole
opening 54 is located adjacent to the accelerating
30 electrodes 50 to form an ion beam. A pair of deflector
electrodes 56 serves to bend the ion beam and direct it
along a fourfold symmetry axis of four rod electrodes 58
of the quadrupole mass spectrometer 4. (Only two of the
rod electrodes 58 are visible in FIG. 1). The rod elec-
35 trodes 58 are connected to control circuitry (not shown)

which provides the conventional DC and radio-frequency
signals which enable quadrupole mass spectrometers to
effect a "mass filtering" of an ion beam. Two beam-offset
electrodes 60 and 62 and an ion multiplier 64 are posi-
5 tioned past a beam-exit end of the four rod electrodes 58.
The beam-offset electrodes steer the mass-filtered ion
beam leaving the four rod electrodes 58 into the ion
multiplier 64 for detection. The interior of the mass
spectrometer 4 is evacuated to a high vacuum through a first
10 evacuation port 66. A region surrounding the accel-
erating electrodes 50 is evacuated to a high vacuum
through a second evacuation port 68.

    Turning now to FIG. 2, an electrically-heated
15 nozzle assembly 100 includes an annular heat-transfer
block 8 surrounding a stainless steel capillary tube 6 as
discussed in connection with FIG. 1. The heat-transfer
block 8 is made of copper and makes thermal contact with
the capillary tube 6. An array of electrically-resistive
20 heating elements 102 are disposed around the heat-transfer
block 8, and are capable of heating the heat-transfer
block 8 to temperatures of up to roughly 1000°C.

    A preferred mode of operation of the ion-vapor
25 source 2 of FIG. 1 will now be described. A solution of
an involatile compound to be mass analyzed dissolved in a
polar solvent such as water or methanol is metered into
the capillary tube 6 and caused to flow towards the
discharge end. Flow rates of from about 0.5 ml/min to
30 about 1 ml/min are preferred for capillaries of the
preferred dimensions set forth above. A length of the
capillary tube 6 is heated to a temperature sufficient to
atomize the solution by the oxy-hydrogen torches 12 of
FIG. 1 or the electrically resistive heating elements 102
35 of FIG. 2. Heating the capillary tube 6 to incandescence,

as high as 1000°C or higher, is generally preferred. Upon
entering the capillary passageway 10 leading through the
heated zone of the capillary tube 6, the solution is
atomized and a mixture of vapor and an aerosol is ejected
5   from the passageway into the spray input subchamber 20.
It is believed that vaporization of the solvent protects
the solute from pyrolysis in passing through the incan-
descent capillary tube 6. The particles of the aerosol
tend to form a beam along the particle beam axis defined
10 by the axis at the discharge end portion 14 of the
capillary tube 6.

The pressure in the spray input subchamber 20 is
maintained at about one torr by pumping with a vacuum pump
15 connected to the first evacuation port 24. Solvent tends
to evaporate, or sublimate, as the case may be, from the
aerosol particles in the reduced pressure environment of
the spray input subchamber 20, thereby increasing the
concentration of the involatile solute in the particles.
20 Preferably only about 5 percent of the solvent relative to
the original solution remains in the particles when the
particles strike the vaporizer surface 46.

A fraction of particles ejected from the
25 capillary passageway 10 of the heat-transfer block 8 pass
through the collimator opening 28 of the skimmer 26 and
into the surface vaporization subchamber 30. The surface
vaporization subchamber 30 is maintained at a pressure
of about 1 torr. The vaporizer surface 46 is heated to a
30 temperature sufficient to vaporize the particles impacting
the surface. Satisfactory operation has been achieved by
maintaining the vaporization surface 46 at about 250°C.
Particles passing through the collimator opening 26 strike
the vaporizer surface 46 and are vaporized to form an ion
35 vapor. It is believed that ordinarily the electric charge

in the ion vapor is for the most part derived from charges
carried by the particles from their formation at the
heated zone of the capillary tube 6. However, additional
charging may possibly take place upon impact vaporization
5 at the vaporization surface 46. Typically a greater
fraction of the solute molecules are ionized in the ion
vapor than are the solvent molecules.

Ion vapor formed at the vaporization surface 46
10 passes through the ion-vapor discharge orifice 54 and
enters the quadrupole mass spectrometer 4 for mass
analysis.

The present invention has only recently been
15 discovered and the various phenomena involved are not yet
fully understood. It is believed tentatively that the
extreme rapidity with which the minute particles of sample
are heated upon striking the vaporizer surface may be a
significant factor in explaining why involatile compounds
20 which decompose upon being heated at more usual slow rates
often yield an ion vapor in the present invention with
little if any evidence of decomposition. In addition, the
sudden vaporization of residual volatile solvent in the
particles may tend to sweep involatile solute molecules
25 into a gaseous phase.

Example

A solution of adenosine 5'-monophosphate (AMP)
30 in a solvent of 0.2 molar formic acid was prepared by
dissolving 0.1 mg of AMP in one milliliter of the solvent.
AMP is a relatively involatile compound which is thermally
labile.

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A liquid chromatograph with the column removed
was connected to the capillary tube 6 of the ion-vapor
source 2 of FIG. 1 to serve as an inlet system for meter-
ing samples into the ion vapor source. A sample of 20 ul
5 of the AMP solution was injected into the liquid chromato-
graph using 0.2 molar formic acid as the liquid phase.
The flow rate was 0.5 ml/min. The heat-transfer block 8
was maintained at roughly 1000°C and the vaporizer surface
46 was heated to about 250°C. Both the spray input
10 subchamber 20 and the surface vaporization subchamber 30
were maintained at a pressure of about one torr.

FIG. 3 presents the resulting mass spectrum. The
spectrum was scanned from about 10 to about 600 amu in
15 about 4 seconds. The most intense peak is of the pro-
tonated molecular ion of AMP. The protonated molecular
ion of this compound was not observed when conventional
chemical ionization was employed. A mass spectrum of AMP
similar to the spectrum of FIG. 3 has been obtained by a
20 field-desorption ionization technique.

The peaks below mass 100 in the mass spectrum
of FIG. 3 are due to the solvent. Considering that the
concentration of AMP in the sample was about 10 parts per
25 million relative to the solvent, the ratio of the inten-
sity of the ions derived from AMP to the intensity of the
solvent ions is amazingly high.

It is not intended to limit the present inven-
30 tion to the specific embodiments described above. For
example, the ion vapor source need not be attached to a
mass analyzer. In this regard, the ion vapor source could
be connected to an ion current meter and serve as a
detector for a liquid chromatograph. Since satisfactory
35 results are obtained with the spray input subchamber 20

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and the surface vaporization subchamber 30 maintained at
about the same pressure, it is expected that the partition
separating the two subchambers could be eliminated. An
electron beam generator could be mounted in the apparatus
5   of FIG. 1 to direct an electron beam into the surface
vaporization subchamber along a direction mutually perpen-
dicular to the particle beam axis and an axis defined by
the support arm 42 of the vaporization probe 40. Such an
electron beam generator could be used to initiate chemical
10 ionization in vapor from the vaporization surface 46, and
would be of particular advantage for solutions with
nonpolar solvents such as hexane. It is recognized that
these and other changes may be made in the apparatus and
method specifically described herein without departing
15 from the scope and teachings of the invention, and it is
intended to encompass all other embodiments, alternatives,
and modifications consistent with the present invention.

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Claims

1. An ion vapor source for obtaining an ion
vapor from a liquid sample, the ion vapor source comprising:

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(a) a source housing having an interior
defining an ionization chamber, an inlet port,
and an ion-vapor discharge orifice;

10

(b) an atomizing nozzle assembly secured
to the inlet port of the source housing, the
atomizing nozzle assembly having a passageway
extending through it for introducing the sample
into the ionization chamber, the passageway

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having a first end defining a liquid-sample
inlet for receiving the liquid sample, and a
second end opening into the ionization chamber,
the second end of the passageway defining a
spray outlet for discharging an aerosol includ-

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ing particles of the sample into the chamber,
at least a portion of the walls of the passage-
way defining a sample heating surface;

(c) a nozzle heater for heating the sample
heating surface of the nozzle assembly to heat

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liquid passing through the passageway of the
atomizing nozzle assembly;

(d) surface vaporizer means for inter-

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cepting particles of sample for vaporization,
the surface vaporizer means having a vaporizer
surface located within the ionization chamber in
the vicinity of the ion vapor discharge orifice,
the vaporizer surface being positioned and

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oriented such that at least a fraction of the

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particles discharged from the spray outlet of
the nozzle assembly are intercepted by the
vaporizer surface, and heat supply means for
maintaining the vaporizer surface at an impact
vaporization temperature such that particles of
sample impinging upon the surface are vaporized to
form an ion vapor for discharge from the ion-vapor
discharge orifice.

2.   The ion vapor source according to claim 1
in which the source housing is generally vacuum tight,
the source housing having an evacuation port connectable to
a vacuum pump for maintaining the ionization chamber at a
pressure in the range of from about 0.1 torr to about 10 torr.

3.   The ion vapor source according to claim 2 in
which the heat supply means of the surface vaporizer means
includes an electrical resistance heating element in a
heat-transfer relationship to the vaporizer surface, the
heating element being capable of maintaining the vaporizer
surface at a temperature of at least about 350°C.

4.   The ion vapor source according to claim 3
in which the atomizing nozzle assembly includes a metal
capillary tube having a capillary channel extending
through it to define the passageway of the nozzle assembly,
the capillary tube being secured to the source housing
in a vacuum-tight manner with the capillary channel of
the capillary tube communicating with the ionization
chamber through the inlet port of the housing; and

in which the atomizing heater means is adapted to heat at
least a portion of the capillary tube to incandescence.

5. The ion vapor source according to claim 4 in which the atomizing heater means includes a torch positioned and oriented so that in operation it directs a flame against the capillary tube block.

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6. The ion vapor source according to claim 5 in which the torch is an oxy-hydrogen torch.

7. The ion vapor source according to claim 4 in which:

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the capillary tube is made of stainless steel; and

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the atomizing heater means includes a plurality of oxy-hydrogen torches disposed generally symmetrically around the capillary tube, each oxy-hydrogen torch being positioned and oriented so that in operation it directs a flame against the capillary tube.

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8. The ion vapor source according to claim 4 in which the atomizing heater means includes an electrical-resistance heating element in a heat transfer relationship to the capillary tube.

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9.   The ion vapor source according to claim 2 in which

the source housing includes a vaporizer-probe port opening into the ionization chamber, and

the surface-vaporizer means includes:

(d.1)   a vaporizer probe extending through the vaporizer probe port of the source housing and into the ionization chamber, the vaporizer probe being joined to the housing in a vacuum-tight manner, the vaporizer probe comprising

(i)   a hollow support arm, and

(ii) a surface-vaporizer end cap joined in a vacuum-tight manner to an end of the support arm, the end cap extending into the ionization chamber and having a generally planar face defining the vaporizer surface, the support arm being positioned and oriented to locate the vaporizer surface in the vicinity of to the ion-vapor discharge orifice and facing in a direction such that in operation at least a fraction of the particles discharged from the spray outlet of the nozzle assembly are intercepted by the vaporizer surface; and

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(d.2) an electrical-resistance heating element
located within the interior of the
vaporizer probe in a heat-transfer
relationship with the end cap for heating
the vaporizer surface.

10. The ion vapor source according to claim 9
in which the vaporizer surface is composed of nickel.

11. The ion vapor source according to claim 2
further comprising:

(e) a collimator partition located within
the ionization chamber, the collimator partition
dividing the ionization chamber into a spray
input subchamber and a surface vaporization sub-
chamber, the spray outlet of the atomizing
nozzle assembly communicating with the spray
input subchamber, the ion vapor discharge
orifice communicating with the surface vaporiza-
tion subchamber, the vaporizer surface being
located in the surface vaporization subchamber,
the collimator partition having a collimator
opening passing through it, the collimator
opening being located along a straight-line path
defined between the spray outlet of the atomizing
nozzle assembly and a target point on the
vaporizer surface so that particles discharged
from the spray outlet passing through the
collimator opening are moving in a direction to
impinge upon the vaporizer surface.

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12.   The ion vapor source according to claim 11 in
which:

5   the collimator partition is secured to
the source housing in a vacuum tight manner so   .
that the spray input subchamber communicates
with the surface vaporization subchamber substan-
tially only through the collimator opening;

10   the evacuation port opens into the spray
input subchamber for maintaining the spray input
subchamber at a subatmospheric presssure;
and

15   the source housing has an auxiliary evacua-
tion port which opens into the surface vaporization
subchamber, the auxiliary evacuation port being
connectable to an auxiliary vacuum pump for
maintaining the surface vaporization subchamber at
20   a pressure in the range of from about 0.1 torr
to about 10 torr.

13.   The ion vapor source according to claim 12
in which the collimator partition at the collimator
25 opening is shaped to form a frustoconical skimmer, the
skimmer being generally circularily symmetric with a
symmetry axis generally coinciding with the straight-line
path defined between the spray outlet of the nozzle
assembly and the target point of the vaporizer surface, a
30 narrow end of the frustoconical skimmer facing the spray
outlet of the nozzle assembly.

14.   The ion vapor source according to claim 2 in
which the atomizer nozzle assembly is electrically grounded.

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15.   The ion vapor source according to claim 2
further comprising:

      (e)   an electron beam generator positioned and
oriented to direct an electron beam into the
ionization chamber in the vicinity of the vaporizer
surface to permit vapor from the vaporization
surface to be ionized by electron impact or chemical
ionization.

16.   A mass spectrometer for mass analyzing liquid
samples comprising:

      (a)   a mass spectrometer having an ion
vapor inlet for receiving ion vapor for mass
analysis; and

      (b)   an ion-vapor source for obtaining an
ion vapor from a liquid sample, the ion vapor
source comprising:

      (b.1)   a source housing attached to the
mass spectrometer, the source housing having
an interior defining an ionization chamber,
an inlet port, and an ion-vapor discharge
orifice communicating between the vacuum
chamber and the ion vapor inlet of the mass
spectrometer;

(b.2)   an atomizing nozzle assembly secured
to the inlet port of the source housing, the
atomizing nozzle assembly having a passageway
extending through it for introducing the
sample into the ionization chamber, the
passageway having a first end defining a
liquid-sample inlet for receiving the liquid
sample, and a second end opening into the
ionization chamber, the second end of the
passageway defining a spray outlet for dis-
charging an atomized spray of vapor and
particles of the sample into the chamber at
least a portion of the walls of the passageway
defining a sample heating surface;

(b.3)   a nozzle heater for heating the
sample heating surface of the nozzle assembly
to heat liquid passing through the passageway
of the atomizing nozzle assembly;

(b.4)   surface vaporizer means for inter-
cepting particles of sample for vaporization,
the surface vaporizer means having a vaporizer
surface located within the ionization chamber
in the vicinity of the ion vapor discharge
orifice, the vaporizer surface being posi-
tioned and oriented such that at least a
fraction of the particles discharged from the
spray outlet of the nozzle assembly are
intercepted by the vaporizer surface, and heat
supply means for maintaining the vaporizer
surface at an impact vaporization temperature
such that particles of sample impinging upon
the surface are vaporized to form an ion vapor

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for discharge from the ion-vapor discharge
orifice into the ion vapor inlet of the mass
spectrometer for mass analysis.

5   17.   The mass spectrometer according to claim 16
in which:

        the source housing of the ion vapor source
is generally vacuum tight, the source having an
10   evacuation port connectable to a vacuum pump for
maintaining the ionization chamber at a pressure
in the range from about 0.1 torr to about 10 torr;

        the heat supply means of the surface
15   vaporizer includes an electrical resistance
heating element in a heat-transfer relationship
to the vaporizer surface; and

        the atomizing nozzle assembly includes a
20   metal capillary tube having a capillary channel
extending through it to define the passageway of
the nozzle assembly; and the capillary tube being
secured to the source housing in a vacuum-tight
manner with the capillary channel of the
25   capillary tube communicating with the ionization
chamber through the inlet port of the housing;
and

in which the atomizing heater means is adapted to heat at
30 least a portion of the capillary tube to incandescence.

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18.   A liquid chromatograph/mass spectrometer
system comprising:

(a)   a liquid chromatograph having a
sample outlet for discharging effluent from the
liquid chromatograph;

(b)   a mass spectrometer having an ion
vapor inlet for receiving ion vapor for mass
analysis; and

(c)   an ion vapor source for interfacing
the liquid chromatograph to the mass spec-
trometer, the ion vapor source comprising:

(c.1)   a source housing attached to the
mass spectrometer, the source housing having
an interior defining an ionization chamber, an
inlet port, and an ion-vapor discharge orifice
communicating between the ionization chamber
and the ion vapor inlet of the mass
spectrometer;

(c.2)   an atomizing nozzle assembly secured
to the inlet port of the source housing, the
atomizing nozzle assembly having a passageway
extending through it for introducing the sample
into the ionization chamber, the passageway
having a first end communicating with
the sample outlet of the liquid chromatograph
for receiving liquid effluent from the chromato-
graph, and a second end opening into the
ionization chamber, the second end of the
passageway defining a spray outlet for dis-
charging an aerosol including particles of the
effluent into the chamber, at least a portion

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of the walls of the passageway defining
a sample heating surface;

(c.3) a nozzle heater for heating the
sample heating surface of the nozzle assembly
to heat the effluent passing through the
passageway of the atomizing nozzle assembly;
and

(c.4) surface vaporizer means for inter-
cepting particles of effluent for vaporization,
the surface vaporizer means having a vaporizer
surface located within the ionization chamber
in the vicinity of the ion vapor discharge
orifice, the vaporizer surface being posi-
tioned and oriented such that at least a
fraction of the particles discharged from the
spray outlet of the nozzle assembly are
intercepted by the vaporizer surface, and heat
supply means for maintaining the vaporizer
surface at an impact-vaporization temperature
such that particles of effluent impinging upon
the surface are vaporized to form an ion vapor
for discharge from the ion-vapor discharge
orifice into the ion vapor inlet of the mass
spectrometer for mass analysis.

19. The liquid chromatograph/mass spectrometer
system according to claim 18 in which:

the source housing is generally vacuum tight,
the source housing having an evacuation port connectable to
a vacuum pump for maintaining the ionization chamber at a
pressure in the range of from about 0.1 torr to about 10
torr;

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the heat supply means of the surface vaporizer
includes an electrical resistance heating element in
a heat-transfer relationship to the vaporizer surface;
and

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the atomizing nozzle assembly includes
a metal capillary tube having a capillary channel extend-
ing through it to define the passageway of the nozzle
assembly, a first end of the capillary tube being con-
nected to the sample outlet of the liquid chromatograph,
10   the capillary tube being secured to the source housing
in a vacuum-tight manner with the capillary channels of
the capillary tube communicating with the ionization
chamber through the inlet port of the housing; and

15
in which the atomizing heater means is adapted to heat at
least a portion of the capillary tube to incandescence.

20   20.   A detector for a liquid chromatograph or
the like, comprising:

(a)   an ion vapor source for obtaining an
ion vapor from liquid effluent from the liquid
25   chromatograph, the ion vapor source comprising:

(a.1)   a source housing having an interior
defining an ionization chamber, an inlet port,
and an ion-vapor discharge orifice;

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(a.2)   an atomizing nozzle assembly secured
to the inlet port of the source housing, the
atomizing nozzle assembly having a passageway
extending through it for introducing the sample
into the ionization chamber, the passageway
having a first end defining a liquid-sample
inlet for receiving liquid effluent from
the liquid chromatograph, and a second end
opening into the ionization chamber, the
second end of the passageway defining a
spray outlet for discharging an aerosol
including particles of the effluent into the
chamber, at least a portion of the walls of
the passageway defining a sample heating
surface;

(a.3)   a nozzle heater for heating the
sample heating surface of the nozzle assembly
to heat the effluent passing through the
atomizing nozzle assembly; and

(a.4)   surface vaporizer means for inter-
cepting particles of sample for vaporization,
the surface vaporizer means having a vaporizer
surface located within the ionization chamber
in the vicinity of the ion vapor discharge
orifice, the vaporizer surface being posi-
tioned and oriented such that at least a
fraction of the particles discharged from the
spray outlet of the nozzle assembly are inter-
cepted by the vaporizer surface, and heat
supply means for maintaining the vaporizer
surface at an impact-vaporization temperature
such that particles of sample impinging upon
the surface are vaporized to form an ion

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vapor for discharge from the ion-vapor dis-
charge orifice; and

(b) an ion-current meter for measuring
the magnitude of an ion current, the ion-current
meter having an ion vapor inlet and a current
magnitude display, the ion vapor inlet being
connected to the ion vapor discharge orifice of
the ion vapor source for receiving ion vapor
discharged from the ion vapor source.

21.   The detector according to claim 20 in which:

the source housing is generally vacuum tight, the
source housing having an evacuation port connectable to a
vacuum pump for maintaining the ionization chamber at a
pressure in the range of from about 0.1 torr to about 10
torr;

the heat supply means of the surface vaporizer
means includes an electrical resistance heating element in
a heat-transfer relationship to the vaporizer surface;

the atomizing nozzle assembly includes a metal
capillary tube having a capillary channel extending through
it to define the passageway of the nozzle assembly, a first
end of the capillary tube being connectable to the sample
outlet of the liquid chromatograph, the capillary tube
being secured to the source housing in a vacuum-tight
manner with the capillary bore of the heat-transfer block
communicating with the ionization chamber through the
inlet port of the housing; and

in which the atomizing heater means is adapted to heat at
least a portion of the capillary tube to incandescence.

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22. A process of generating an ion vapor from a
sample of liquid solution, the solution including a solute
and a polar solvent, the process comprising the steps of:

5   (a) metering the solution into a first end
of a capillary passageway;

           (b) heating walls of a lengh of the passage-
way to incandescense to atomize the solution, the
10   rate at which the solution is introduced into the
passageway and the temperature of the walls
being selected so that a mixture of vapor and
particles from the solution are discharged from
a second end of the passageway, at least a
15   fraction of the particles being electrically
charged;

           (c) maintaining a substantially enclosed
region at a subatmospheric pressure by evacuating
20   the region with a vacuum pump;

           (d) introducing at least a fraction of the
vapor and particles discharged from the capillary
passageway into the subatmospheric-pressure
25   region to pump away a portion of the vapor with
the vacuum pump;

           (e) heating a vaporization surface to a
temperature above an impact vaporization temper-
30   ature of the particles at the subatmospheric
pressure; and

           (f) directing at least a fraction of the
charged particles in the subatmospheric-pressure
35   region to impinge upon the heated vaporization
surface to be vaporized to form the ion vapor.

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22.   The process according to claim 21 in which
the pressure in the subatmospheric-pressure region is
maintained at roughly 1 torr.

5   23.   The process according to claim 22 in which a
length of the capillary passageway passes through a copper
heat-transfer block, and in which the step (b) of heating
the walls of a length of the passageway includes the step
of heating the heat-transfer block to a temperature of
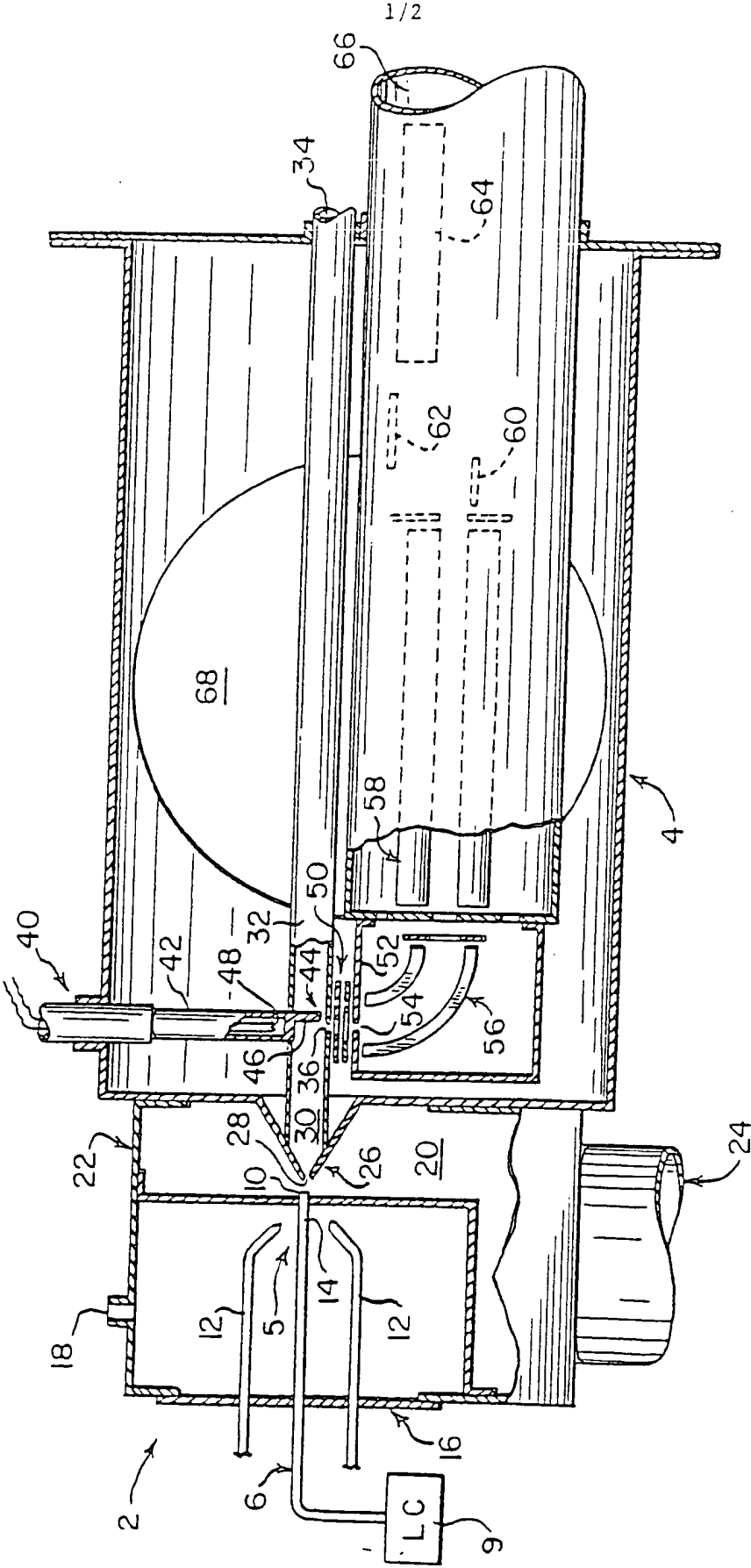10   roughly 1000°C.

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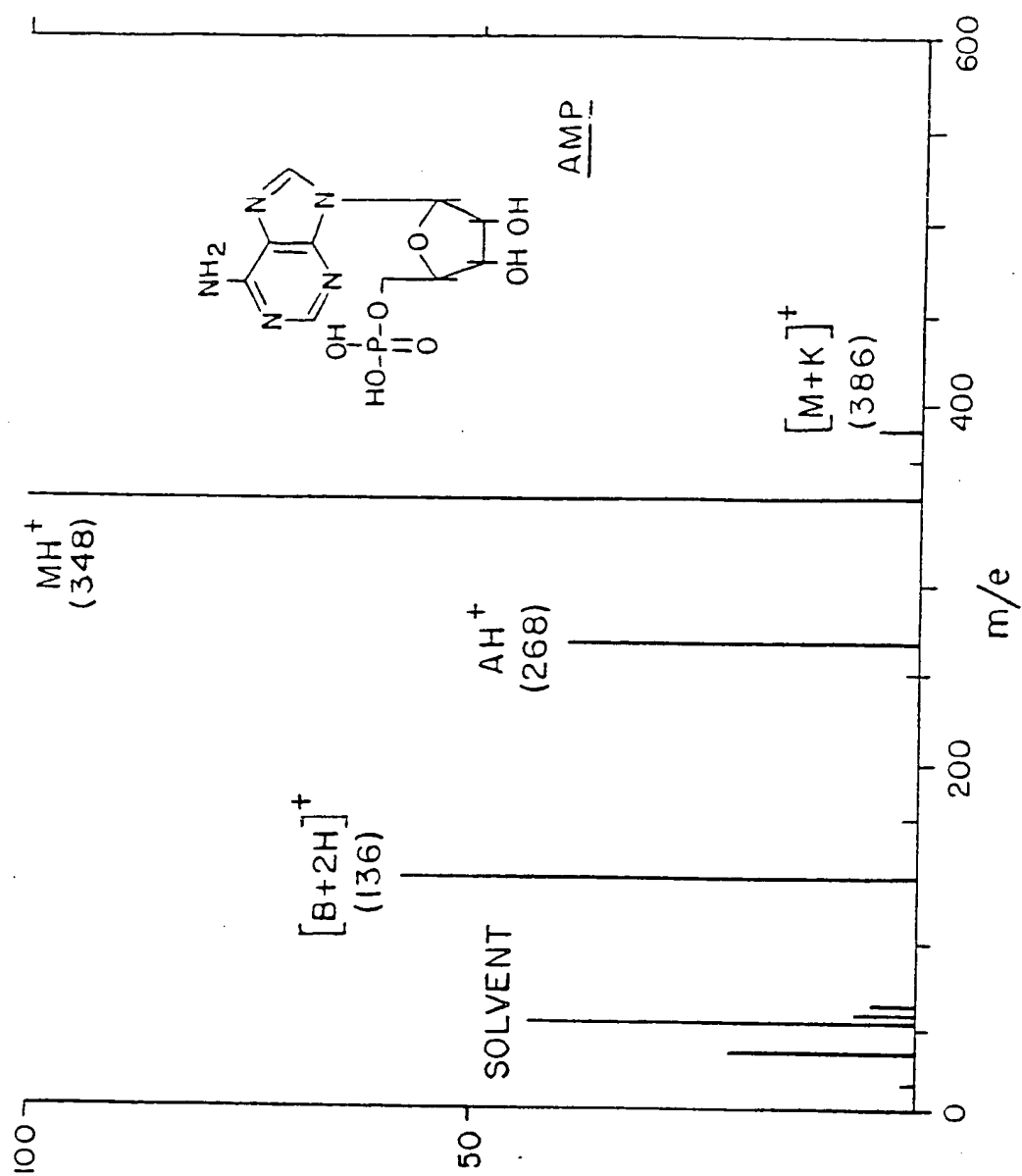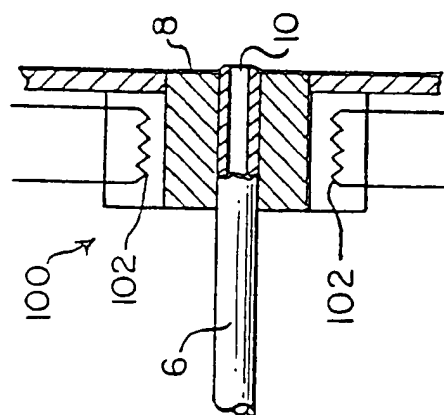
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FIG. 1

FIG. 3

FIG. 2

INTERNATIONAL SEARCH REPORT

International Application No   PCT/US81/00693

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ³

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL.³ H01J 49/28
US. CL.   250/281

II. FIELDS SEARCHED

Minimum Documentation Searched ⁴

Classification System	Classification Symbols
U.S.	250/281, 250/423, 250/425, 250/288 73/61.3, 73/61.1C

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are included in the Fields Searched ⁵

III. DOCUMENTS CONSIDERED TO BE RELEVANT ¹⁴

Category *	Citation of Document, ¹⁶ with indication, where appropriate, of the relevant passages ¹⁷	Relevant to Claim No. ¹⁸
X,T	N, ANALYTICAL CHEMISTRY, VOL. 52, No. 11, BLAKLEY et al: LIQUID CHROMATOGRAPH-MASS SPECTROMETER FOR ANALYSIS OF NONVOLATILE SAMPLES page 1636-1641, issued September, 1980	
A,	US, A, 4,160,161, Published 3 July 1979, HORTON	
A	US, A, 4,055,987, Published 1 November 1977, McFADDEN	
A	US, A, 4,144,451, Published 3 March 1979, KAMBARA	
A	US, A, 2,621,296, Published 9 December 1952, THOMPSON	
A	US, A, 3,336,475, Published 15 August 1967, KILPATRICK	

* Special categories of cited documents: ¹⁵

"A" document defining the general state of the art

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"P" document published prior to the international filing date but on or after the priority date claimed

"T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention

"X" document of particular relevance

IV. CERTIFICATION

Date of the Actual Completion of the International Search ²	Date of Mailing of this International Search Report ²
11 August, 1981	18 AUG 1981

International Searching Authority ¹	Signature of Authorized Officer ²⁰
ISA/US	H. A. Dixon

Form PCT/ISA/210 (second sheet) (October 1977)